IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NATURAL ALTERNATIVES INTERNATIONAL, INC., ET AL., Plaintiffs, v. VITAL PHARMACEUTICALS, INC., and DNP INTERNATIONAL CO., INC., Defendants.	)	C.A. No. 09-626-GMS
VITAL PHARMACEUTICALS, INC., Counterclaim / Third-Party Plaintiff, v. NATURAL ALTERNATIVES INTERNATIONAL, INC., and COMPOUND SOLUTIONS, INC., Counterclaim / Third-Party Defendants.	)	

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

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I. INTRODUCTION

Defendants Vital Pharmaceuticals, Inc. ("VPX") and DNP International Co. ("DNP") (collectively, "Defendants") jointly submit their opening claim construction brief.

In this case, the inventors received broad patent claims that cover the ingestion of well-known compositions that include beta-alanine and L-histidine, and the subsequent accumulation of beta-alanylhistidine and creatine in tissues. Having intentionally obtained these claims, but now seeking to prevent invalidation, Plaintiffs ask the Court to narrow—not broaden—the scope of their claims. In doing so, Plaintiffs offer arguments that run directly afoul of the canons of claim construction.

Defendants, on the other hand, offer clear constructions that are either taken directly from the definitional language used by the inventors, or are compelled by the plain meaning of the claim language as understood by one of ordinary skill in the art, and supported by the specification, the prosecution history, and extrinsic evidence. Defendants' constructions should be adopted.

II. STATEMENT OF FACTS

A. Background of the Technology

The patents-in-suit, U.S. Patent Nos. 6,426,361 ("the '361 patent"), 6,172,098 ("the '098 patent"), and 5,965,596 ("the '596 patent"),[1] all belong to the same family of patents and all appear to have a common specification.[2] The patents are directed to methods and compositions for increasing the concentration of beta-alanylhistidine dipeptide in tissue, thereby purportedly increasing the anaerobic working capacity of such tissue. *See* col. 2, lns. 25-38. The

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[1] A copy of the '361 patent, the '098 patent, and the '596 patent can be found in the Joint Appendix ("J.A.") at Exs. 1, 2, and 3 respectively.

[2] The citations to the specification by col. ___, ln. __ herein refer to the column and line numbers in the '361 patent.

compositions include dietary supplements that comprise beta-alanine and L-histidine. Col. 3, lns. 40-42. The methods of the patents-in-suit include, among other things, providing beta-alanine and L-histidine to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in a tissue. Col. 2, ln. 61 – col. 3, ln. 3.

To understand the subject of the patents-in-suit, it is helpful to first understand the meaning of some common biochemical terms. As described in the Declaration of Dr. Malcolm Watford ("Watford Decl.") ¶¶ 9-12, a dipeptide is a molecule consisting of two amino acids joined together by a peptide bond. Carnosine, which is used throughout the patents-in-suit and is also referred to as beta-alanyl-L-histidine or beta-alanylhistidine, is a dipeptide consisting of the amino acids beta-alanine and L-histidine. *Id.* This table provides a visual explanation:

β-Alanine	**Beta-alanine** (an amino acid)
L-Histidine	**L-Histidine** (an amino acid)
[(β-Alanine)—(L-Histidine)]	**Carnosine** (a dipeptide consisting of beta-alanine and L-histidine joined by a peptide bond).

B. Claim Terms to be Construed

NAII has alleged infringement of claims 5-7, 17-20, and 32-33 of the '361 patent, claim 11 of the '098 patent, and claims 1-7 and 9-11 of the '596 patent.[3] The Joint Claim Construction Chart (D.I. 74) lists the disputed claim terms and the parties' constructions.[4]

III. PRINCIPLES OF CLAIM CONSTRUCTION

Claim construction is a matter of law and a threshold issue for the trial court to decide. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370, 372 (1996). The court determines the meaning of pertinent claim language to establish

[3] A copy of each of the claims asserted against VPX with the disputed claim terms indicated in bold-face type is attached as Exhibit A to the Declaration of Keith A. Walter ("Walter Decl.").

[4] The parties agreed that the term "mixture" as used in claims 5 and 17 of the '361 patent means "a composition, physical combination, or blend of substances that are not chemically bonded to one another," and thus, does not need to be construed by this Court.

the scope of the claims for purposes of determining infringement and validity. *Id.* at 978-79. There are four principal sources of evidence that the trial court may use in construing claims: (1) the language of the claims; (2) the patent specification; (3) the prosecution history; and (4) extrinsic evidence. Claim construction begins with an examination of the intrinsic evidence, *i.e.*, sources (1)-(3) above. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). Intrinsic evidence is preferred and is the most useful in claim construction. Although extrinsic evidence can be used, it is considered secondary. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1318-19 (Fed. Cir. 2005) (*en banc*).

A. The Starting Point for Claim Construction Is the Language of the Claims

The claims of a patent "define the invention to which the patentee is entitled the right to exclude." *Phillips*, 415 F.3d at 1312 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). Because the language used in the claims determines the scope of the invention, claim construction "begin[s] and remain[s] centered on the language of the claims themselves, for it is that language that the patentee chose to use." *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001).

B. Claims Must Be Read in Light of the Specification

The claims must also "be read in view of the specification, of which they are a part." *Phillips*, 415 F.3d at 1315. "[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics*, 90 F.3d at 1582. "[Where a] patentee has clearly defined a claim term, that definition usually is dispositive; it is the single best guide to the meaning of [the] term." *Guttman, Inc. v Kopykake Enters., Inc.*, 302 F.3d 1352, 1360 (Fed. Cir. 2002). The specification, however, cannot be used as a source of claim limitations that do not appear in the claims themselves. *Gart v. Logitech, Inc.*, 254 F.3d 1334, 1343 (Fed Cir. 2001).

C. Prosecution History May Inform Construction

In addition to the language of the claims and the specification, a Court "should also consider the patent's prosecution history, if it is in evidence." *Phillips*, 415 F.3d at 1317 (*quoting Markman*, 52 F.3d at 980). "Yet because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* As a result, there is a "heavy presumption" that claim terms carry their full ordinary and customary meaning, even when evaluating prosecution history statements. *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323 (Fed. Cir. 2003).

D. Extrinsic Evidence Can Be Used to Assist the Court

Extrinsic evidence, such as expert testimony and dictionaries, can be used if needed to determine the meaning or scope of technical terms in the claims. *Vitronics*, 90 F.3d at 1583.

IV. CONSTRUCTION OF THE DISPUTED TERMS

A. "beta-alanine" and "L-histidine" ('361 Patent [claims 5, 17, 32 and 33]; '098 Patent [claim 5]; and '596 Patent claims [1, 2, 4, 6, 7, and 10])

Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"**beta-alanine**" means "the individual amino acid, beta-alanine, or its salt, ester or amide" "**L-histidine**" means "the individual amino acid, L-histidine, or its salt, ester, or amide"	"**beta-alanine**" means "beta-alanine in the form of the individual amino acid, or as a component of a dipeptide (such as carnosine), an oligopeptide, or a polypeptide, or an active derivative thereof" "**L-histidine**" means "L-histidine in the form of the individual amino acid, or as a component of a dipeptide (such as carnosine), an oligopeptide, or a polypeptide, or an active derivative thereof"

The inventors provided clear and deliberate definitions of "beta-alanine" and "L-histidine" in the specifications of the patents-in-suit. Defendants' proposed constructions of "beta-alanine" and "L-histidine" merely, and appropriately, adopt those definitions.

In the "Summary of the Invention" portion of the patents-in-suit, the inventors provided definitions of "beta-alanine" and "L-histidine" that make clear that those terms *are not limited to the individual amino acids beta-alanine and L-histidine*, but also encompass beta-alanine and L-histidine *in the form of components of dipeptides, oligopeptides, or polypepetides, as well as active derivatives thereof.* Specifically, the inventors defined "beta-alanine" and "L-histidine" in the context of their invention as follows:

> The compositions include mixtures of creatine and beta-alanine, creatine, beta-alanine and L-histidine, or creatine and active derivatives of beta-alanine or L-histidine. **Each of the beta-alanine or L-histidine can be in the form of the individual amino acids, or components of dipeptides, oligopeptides, or polypeptides.** The beta-alanine or L-histidine can be active derivatives.

Col. 2, lns. 40-46 (emphasis added). This definition governs the construction of the terms "beta-alanine" and "L-histidine." The definition unmistakably indicates that the terms "beta-alanine" and "L-histidine" refer to beta-alanine and L-histidine in either (a) the individual amino acid form or (b) as a component of either a dipeptide, an oligopeptide, or a polypeptide. It also unmistakably indicates that the terms encompass active derivatives. The Federal Circuit holds that where the inventors define a claim term in the specification, that definition governs. *See, e.g., Phillips*, 415 F.3d at 1316 (where the specification reveals a particular definition given to a claim term by the inventors, "the inventor's lexicography governs").

The inventors used the terms "beta-alanine" and "L-histidine" consistently with this definition throughout the specification. In the "Background of the Invention" section, the patent specification states that "[d]ipeptides of beta-alanine and histidine . . . include carnosine . . . , anserine . . . , or balenine . . . ." Col. 2, lns. 1-2. This indicates that the terms "beta-alanine" and "histidine" encompass beta-alanine and histidine in the dipeptide form.

Similarly, the patents' "Example 2" describes a study of the effect of supplementing a diet with multiple daily doses of beta-alanine and L-histidine on the carnosine content of human

skeletal muscle. Col. 10, li. 20 – col. 11, li. 60. In that study, chicken broth was used as one source of "beta-alanine." In calculating the total "beta-alanine" content of the broth, the inventors considered both *free beta-alanine* and the beta-alanine components of *beta-alanyl-dipeptides* (*e.g.*, the dipeptides carnosine and anserine) as "beta-alanine." The inventors stated:

> In one session, 8 milliliters per kilogram body weight of broth containing approximately 40 milligrams per kilogram body weight of *beta-alanine (e.g., in the form of anserine and carnosine)* was ingested. For a subject weighing 75 kilograms this amounted to the ingestion of 600 milliliters of broth containing 3 grams of beta-alanine.

Col. 10, ln. 64 – col. 11, ln. 2 (emphasis added). This again demonstrates that the inventors understood and specifically contemplated that *the term "beta-alanine" encompasses beta-alanine in the form of a dipeptide such as carnosine and anserine.*

Another source of "beta-alanine" in the study set forth in Example 2 was pure carnosine (a dipeptide). The patent states that "[a]dministration of *carnosine* equivalent to 20 milligrams per kilogram body weight of *beta-alanine* in one test subject resulted in an equivalent increase in the plasma beta-alanine concentration." Col. 11, lns. 47-52. The inventors presented the results of their study in Table 4, which further confirms that they understood that the term "beta-alanine" encompassed dipeptides. According to the inventors, Table 4 summarizes the inventors' "beta-alanine" absorption study, and shows the estimated equivalent does of beta-alanine for each of the sources of beta-alanine (including the dipeptide carnosine and broth containing beta-alanyl-dipeptides) used in the study. Specifically the specification states that "Table 4 summarizes the allocation of treatments during the beta-alanine absorption study. The estimated equivalent doses of beta-alanine are presented in Table [4]." Col. 11, lns. 21-23.

Perhaps most importantly, the patent claims themselves confirm that the term "beta-alanine" is not limited merely to the individual amino acid, but that it also encompasses the beta-alanine component of a dipeptide (or polypeptide). Claims 3, 12, and 24 of the '361 patent,

which depend from independent claims 1, 10, and 22 respectively, unambiguously demonstrate that the term "beta-alanine" encompasses the beta-alanine component of a dipeptide (or polypeptide). An examination of independent claim 1 and its dependent claim 3 illustrate this unavoidable conclusion:

> 1. A composition comprising a mixture of a creatine and a composition comprising an amino acid or an active derivative thereof selected from the group consisting of ***a beta-alanine***, an ester of a beta-alanine and an amide of a beta-alanine.
>
> 3. The composition of claim 1, ***wherein the beta-alanine further comprises a dipeptide, an oligopeptide, or a polypeptide***.

'361 patent, claims 1 and 3 (emphasis added). Claim 3 compels the conclusion that "beta-alanine" can exist as a component of a dipeptide, an oligopeptide, or a polypeptide; indeed, claim 3 *requires* that it exist in such a form. *See also* '361 claims 12 and 24. Claim terms should be construed consistently throughout a patent. Thus, in *all* of the claims of the '361 patent, when the term "beta-alanine" is used, that term encompasses beta-alanine as a component of a dipeptide, an oligopeptide, or a polypeptide.

Moreover, *dependent* claim 3 must be construed to be narrower than *independent* claim 1 (from which claim 3 depends). *See Intamin, Ltd. v. Magnetar Techs., Corp.*, 483 F.3d 1328, 1335 (Fed. Cir. 2007) ("An independent claim impliedly embraces more subject matter than its narrower dependent claim."). Claim 3 *narrows* the scope of the composition of claim 1. Claim 1 allows the beta-alanine to exist in any form (including the form of a monopeptide, or as a component of a dipeptide, an oligopeptide, or a polypeptide); while claim 3 requires that the beta-alanine be in the form of a component of a dipeptide, an oligopeptide, or a polypeptide. This means that dipeptides, oligopeptides, and polypeptides are necessarily within the scope of the term "beta-alanine" as recited in the claims; otherwise, dependent claims 3, 12, and 24 would not narrow the scope of claims 1, 10, and 22, the independent claims from which these claims

depend, respectively. Thus, Defendants' claim construction—which embraces this concept—should be adopted, while Plaintiffs' construction—which contravenes it—should be rejected.

Extrinsic evidence further supports Defendants' construction of "beta-alanine" and "L-histidine." The inventors' publications evidence that the term "beta-alanine" encompasses beta-alanine in dipeptide form. *See, e.g.,* R.C. Harris, M. Dunnett, *et. al.*, *Changes in plasma beta-alanine (βAla) concentration following administration of free or peptide bound forms*, Experimental Biology 2003, San Diego, California, April 11-15, 2003, Abstract 177.6 ("We investigated the absorption of βAla when administered in the *free or dipeptide* bound form.") (emphasis added) (Walter Decl. Ex. B); R.C. Harris, *et. al.*, *The absorption of orally supplied β-alanine and its effect on muscle carnosine synthesis in human vastus lateralis*, 30 Amino Acids 279, 280 (2006) (referring to "β-alanine in the form of anserine and carnosine") (Walter Decl. Ex. C). Likewise, Dr. Malcolm Watford, a Professor of Nutritional Sciences at Rutgers University, concurs that a person of ordinary skill in the art would have understood the terms "beta-alanine" and "L-histidine" to encompass beta-alanine and L-histidine in any of the free amino acid (monopeptide), dipeptide, oligopeptide, or polypeptide forms. *See* Watford Decl. ¶ 12; *see also, e.g.*, U.S. 5,585,396 at col. 2, lns. 12-14 ("Carnosine ... is a dipeptide composed of the amino acids beta-alanine and histidine.") (Walter Decl. Ex. I).

In contrast to Defendants' constructions of "beta-alanine" and "L-histidine," Plaintiffs' constructions improperly narrow the terms "beta-alanine" and "L-histidine" to only "*the individual amino acid[s]*" *and their salts, esters and amides*.[5] Plaintiffs' construction contravenes the definition of those terms set forth in the specification, the consistent use of those definitions in the specification and the claims, and the extrinsic evidence.

[5] As set forth in the specification, "esters" and "amides" are examples of active derivatives. Col. 2, ln. 50. The term "salts" is not mentioned in any of the patents-in-suit.

In support of their construction, it appears that Plaintiffs intend to rely upon a statement that the inventors made in a "Petition to Make Special" submitted during the prosecution of the '596 patent. Specifically, the inventors stated:

> In contrast to the present invention, the compositions and methods described in Setra's invention teaches dipeptides.
>
> In the present invention, β-alanine and/or L-histidine are administered to regulate hydronium ion concentrations. Setra does not teach, suggest, or mention using monopeptides for the treatment of hydronium ions.

J.A. at Ex. 4, March 4, 1999 Petition to Make Special at 4. To the extent NAII reads this passage to suggest that the inventors narrowed the definition of "beta-alanine" and "L-histidine" to exclude beta-alanine and L-histidine as components of dipeptides, such a reading is misplaced. For example, such a reading is contrary to the applicants' description of the invention on page 3 of *that very same Petition to Make Special*, in which the applicants state that "[t]he methods of the present invention include providing the dipeptides, peptides or peptide analogues by any number of means including, for example, ingestion and injection." J.A. at Ex. 4, March 4, 1999 Petition to Make Special at 3.

In addition, in the subsequent prosecution history of the '361 patent, applicants expressly relied upon the portion of the specification that defines "beta-alanine" and "L-histidine" to include beta-alanine or L-histidine as components of dipeptides, oligopeptides, or polypeptides, as support for newly added claims, which as discussed above, specifically claimed beta-alanine and L-histidine both in the form of the individual amino acids, as well as in the form of dipeptides. In particular, the inventors stated that "[s]upport for new claims directed to a composition wherein the beta-alanine further comprises a dipeptide, an oligopeptide, or a polypeptide can be found, *inter alia*, on [Application] page 3, line 28 to page 4, line 2 [which corresponds to the definitional passage, '361 patent, col. 2, lns. 40-56]." J.A at Ex. 5, August 3, 2001 Response and Amendment at 7.

Accordingly, the inventors' statements in the Petition to Make Special, especially in view of other portions of the prosecution history, do not amount to a clear and unmistakable disavowal of the definition of beta-alanine and L-histidine set forth in the specification. *See, e.g., Purdue Pharma L.P. v. Endo Pharms., Inc.*, 438 F.3d 1123, 1136 (Fed. Cir. 2006) ("Under the doctrine of prosecution disclaimer, a patentee may limit the meaning of a claim term by making a clear and unmistakable disavowal of scope during prosecution."). Moreover, "when the prosecution history appears in conflict with the specification, any ambiguity must be resolved in favor of the specification." *Lydall Thermal/Acoustical, Inc. v. Federal-Mogul Corp.*, No. 2009-1135, 2009 WL 2893190, *6 (Fed. Cir. Sept. 8, 2009) (nonprecedential); *Telecordia Techs., Inc. v. Cisco Sys., Inc.*, 612 F.3d 1365, 1375 (Fed. Cir. 2010) ("These prosecution history comments cannot trump the plain language of the claims and the direct teaching of the specification.")

Thus, because Defendants' constructions of the terms "beta-alanine" and "L-histidine" conform to the inventors' own definitions, Defendants' constructions should be adopted.

B. "dietary supplement" ('361 Patent [claims 5-7, 17-20, and 32-33])

Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"an addition to the normal diet in a pill, capsule, tablet, powder, or liquid form, which is not a conventional food, and effectively increases the function of tissues when consumed"	"a product or substance that is added to the diet"

The parties' dispute over the proper construction of "dietary supplement" centers on whether the Court should deviate from the ordinary meaning of dietary supplement by limiting it—as Plaintiffs advocate—only to certain forms (*e.g.*, pills, capsules, tablets) that are not a conventional food and that must effectively increase the function of tissues when consumed. Defendants' proposed construction, which does not so limit the term, is the correct one. *See Phillips*, 45 F.3d at 1316 ("The construction that stays true to the claim language and most

naturally aligns with the patent's description of the inventions will be, in the end, the correct construction."). Plaintiffs' construction finds no support in the intrinsic record.

Defendants' proposed construction, namely, that dietary supplement means "a product or substance that is added to the diet," is properly derived from the ordinary meaning of the claim language, taking into account the intrinsic record. The specification repeatedly describes dietary supplements as products or substances added to the diet. *See, e.g.,* col. 1, lns. 18-20 ("Natural food supplements are typically designed to compensate for reduced levels of nutrients in the modern human and animal diet."); col. 6, lns. 56-60 ("During the supplementation period an identical feeding regime was implemented. However, each hard feed meal was supplemented with beta-alanine and L-histidine (free base)."). Defendants' construction is also consistent with Webster's, which defines "dietary" to mean "of or relating to a diet" and "supplement" to mean "something that completes or makes an addition." Merriam-Webster's Collegiate Dictionary (10th ed. 1996) (Walter Decl. Ex. D).

Plaintiffs' construction has numerous significant flaws. First, there is no support in the intrinsic record for the notion that a dietary supplement must be in "pill, capsule, tablet, powder, or liquid form, which is not a conventional food." To the contrary, the specification repeatedly describes dietary supplements as being exactly the opposite of Plaintiffs' proposal, namely conventional food not limited to those forms. In Example 2, the inventors describe supplementing the diets of a test subject with chicken broth, which is a conventional food. Col. 10, ln. 23 – col. 11, ln. 11 [Example 2]; col. 11, ln. 56 ("broth, a natural food"); *see also, e.g.,* col. 1, lns. 18-20; col. 6, lns. 56-60.

Second, the intrinsic record does not support Plaintiffs' argument that a dietary supplement must "effectively increase[] the function of tissues when consumed." Again, to the contrary, the specification describes a dietary supplement as being "typically designed to

compensate for reduced levels of nutrients in the modern human and animal diet." Col. 1, lns. 18-20.

Lastly, without any support, Plaintiffs further refine their proposed definition by inclusion of the subjective terms "normal diet" and "conventional food." The specification recognizes that "normal" diets vary: "It can be particularly important to supplement the diets of particular classes of animals whose the [sic] normal diet may be deficient in nutrients available only from meat and animal produce (*e.g.*, human vegetarians and other animals [that] consume an herbivorous diet)." Col. 1, lns. 21-25. Similarly, what constitutes a "conventional" food also depends greatly on subjective opinion. Plaintiffs' addition of these terms make their proposed construction highly subjective and unclear. It, therefore, should be rejected. *See, e.g., Datamize LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1350 (Fed. Cir. 2005) (holding claim indefinite when term is "completely dependent on a person's subjective opinion").[6]

In sum, Defendants' construction is the correct one because, unlike Plaintiffs' construction, it does not deviate from the ordinary meaning or limit the term without support.

C. "active derivative" ('361 Patent [claims 5-7, 17-20, and 32-33])

Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"a compound derived from, or a precursor of, the substance that performs in the same or similar way in the body as the substance, or which is processed into the substance and placed into the body, and excludes dipeptides, oligopeptides and polypeptides"	"a compound derived from, or a precursor of, the substance that performs in the same or similar way in the body as the substance, or which is processed into the substance and placed into the body"

The parties proposed constructions of "active derivative" are similar, but differ in that Plaintiffs' proposed definition deviates in one significant way from the express definition in the specification. The inventors expressly defined the term "active derivative" in the Summary of

[6] Plaintiffs' construction also includes ambiguous and undefined phrases "effectively increases" and "function of tissues" that do not help clarify the claim language but rather add more terms that likely require construction and refinement as trial nears.

Invention: "An active derivative is a compound derived from, or a precursor of, the substance that performs in the same or similar way in the body as the substance, or which is processed into the substance and placed into the body." Col. 2, lns. 46-49. That is the definition which Defendants have proposed—verbatim—and that is the definition which the Court should adopt.

Plaintiffs' construction wrongly adds a limitation to the specification's express definition of active derivative by excluding dipeptides, oligopeptides, and polypeptides. When the inventor has clearly and explicitly defined a claim term in the specification, the rule against importing limitations from elsewhere must be "strictly enforced against adding additional unstated limitations." *3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1369, 1372-73 (Fed. Cir. 2003) (holding that the inventor acted as own lexicographer by stating that "'[m]ultiple embossed' means two or more embossing patterns are superimposed on the web to create a complex pattern of differing depths of embossing," and that district court erred by including a serial embossing step shown in the specification as an additional claim requirement). Because the inventors explicitly defined active derivative in the specification, Plaintiffs' additional limitation to that definition is improper.

In addition, Plaintiffs' construction relies on an ambiguous statement made by the applicants during prosecution of unrelated method claims. Yet, the composition claims were not at issue when the statement was made. The Federal Circuit cautions against relying on such statements. For example, in *Golight, Inc. v. Wal-Mart Stores, Inc.*, 355 F.3d 1327, 1332 (Fed. Cir. 2004), a claim to a "rotating" spotlight was not found subject to a disclaimer where statements in the prosecution history referring to the spotlight rotating "through 360" were made in the context of other claims, not the claim at issue. *See also LG Elecs., Inc. v. Bizcom Elecs., Inc.*, 453 F.3d 1364, 1373-74 (Fed. Cir. 2006) (prosecution history statements that the prior art did not teach accessing data signals "over a system bus" were found not sufficiently clear to

justify limiting claims to required claimed signals to travel over a system).

Here, the prosecution history statement referring to the invention as "using monopeptides for the treatment of hydronium ions" is not only ambiguous, but is attributable *only* to the claims prosecuted in the '596 patent, drawn to a method of regulating hydronium ion concentrations in human tissue. The term "active derivative" is found only in the claims of the '361 patent, which are drawn to compositions. These different inventions (methods versus compositions) were separately prosecuted after the PTO mailed a restriction requirement to the applicants on August 31, 1998. J.A. at Ex. 6, Aug. 31, 1998 Office Action. The prosecution history statement here is not a disclaimer relevant to the composition claims which include the term "active derivative" because, like in *Golight*, the statement is attributable to other claims which are not at issue. In any event, the prosecution history statement is not a clear or express statement that "active derivative" should *not* be defined as it is in the specification.

Finally, Plaintiffs' construction is also wrong because the definition of active derivative cannot exclude dipeptides, oligopeptides, and polypeptides without excluding embodiments of compositions described in the specification. *See On-Line Techs., Inc. v. Bodenseewerk Perkin-Elmer GmbH*, 386 F.3d 1133, 1138 (Fed. Cir. 2004) ("[A] claim interpretation that excludes a preferred embodiment from the scope of the claim is rarely, if ever, correct.") The preferred embodiments include compositions that include dipeptides—specifically beta-alanyl-dipeptides such as carnosine and anserine—that upon administration increase the plasma concentration of monopeptides, specifically beta-alanine and L-histidine monopeptides. *See* col. 5, lns. 11-16; Example 2, col. 10, lns. 43-50; col. 11, lns. 48-52; col. 11, lns. 44-52; Fig 8. Under Plaintiffs' construction of "active derivative," the claims would improperly exclude such embodiments described in the specification.

D. "unit dosage form" ('361 Patent [claims 6 and 18])

Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"doses of a certain serving size that can be taken all at once, or in multiple parts throughout the day"	"a form in which a single dose is contained by itself in a single unit"

Defendants' construction of "unit dose form" is compelled by the plain meaning of the claim language. The term "unit dose form" appears in three dependent claims of the '361 patent (6, 18, and 28), and reference is further made to these claims in further dependent claims. The following is exemplary:

> 6. The dietary supplement of claim 5 in a **unit dosage form**.
>
> 7. The dietary supplement of claim 6, wherein **one dose** comprises up to 99% by weight of beta-alanine.
>
> 8. The dietary supplement of claim 6, wherein **one dose** comprises up to 98% by weight of L-histidine.

'361 patent, claims 6-8 (emphasis added); *see also* claims 18-20, 28-30.

Dependent claims 7 and 8 refer back to the "unit dosage form" claim, and prescribe what "one dose" comprises. This claim language supports a construction of "unit dosage form" as meaning "a form in which a single dose is contained by itself in a single unit," as Defendants have proposed. Such a definition comports with the plain meaning of "unit dosage form."

"Generally, there is a 'heavy presumption' that claim terms carry their ordinary meaning as understood by one of ordinary skill in the art." *PHT Corp. v. Invivodata, Inc.*, Civ. No. 04-60-GMS, 2005 WL 1189552, *1 (D. Del. May 19, 2005) (*quoting CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002), and *citing Vitronics*, 90 F.3d at 1582). "In this regard, pertinent art 'dictionaries, encyclopedias and treatises . . . are objective resources that serve as reliable sources of information on the established meanings that would have been

attributed to the terms of the claims by those of skill in the art.'" *Id.* (*quoting Texas Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1202-03 (Fed. Cir. 2002)).

Pertinent art dictionary definitions of "unit dose form" support the construction of "unit dose form" as meaning "a form in which a single dose is contained by itself in a single unit," as Defendants propose. Several medical dictionaries define "unit dose" as "[a] single dose of a drug provided in an individual labeled packet, container, or syringe." International Dictionary of Medicine and Biology (1986) at vol. 1, p. 856 (Walter Decl. Ex. E); Churchill's Illustrated Medical Dictionary (1989) at p. 560 (Walter Decl. Ex. F). Another medical dictionary defines "unit dose" as "a method of preparing medications in which individual doses of patient medications are prepared by the pharmacy and delivered in individual labeled packets to the patient's unit to be administered by the nurses on the ordered schedule." Mosby's Medical, Nursing, and Allied Health Dictionary (1994) at p. 1614 (Walter Decl. Ex. G). Another pharmaceutical dictionary defines "unit dose" as a "system in which each individual dose is prepared (pre-packaged) beforehand; provides for a more adequate control of drug dispensing." Dictionary of Pharmacy (1986) at p. 309 (Walter Decl. Ex. H).

The plain language of the term, and all of the dictionary definitions, embody the concept that unit dosage form is where *a single dose is contained in its own individual unit* (*e.g.*, a packet, container, or pill). This is precisely what Defendants' proposed construction conveys.

E. "providing an amount of [beta-alanine or L-histidine] to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in a human tissue" ('098 Patent [claim 5]; '596 Patent [claims 1, 2, 4, 6, and 10])

Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"supplying to a human an amount of [beta-alanine or L-histidine] by ingestion and therefore, causing an increase in [beta-alanine or L-histidine] in blood or blood plasma above normal concentrations found in a typical fed state, and thereby increasing the	"directly or indirectly providing an amount of [beta-alanine or L-histidine] to the blood or blood plasma that increases beta-alanylhistidine dipeptide synthesis in a human tissue"

synthesis of beta-alanylhistidine dipeptide in the tissue"	

The dispute between the parties' constructions of "providing an amount of [beta-alanine or L-histidine] to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in a human tissue" is whether the Court should deviate from the otherwise ordinary meaning of "providing" by construing it to mean providing *only by ingestion.* Defendants' construction, which does *not* so limit the term "providing," is the correct one.

First, because the inventors did not express the intent to deviate from the ordinary meaning of "providing," or otherwise limit their use of the word to mean "providing by ingestion," the Court should not so limit the term beyond its ordinary meaning. *See, e.g., Univ. of Pittsburgh v. Hedrick*, 573 F.3d 1290, 1296 (Fed. Cir. 2009) ("The specification may impart a definition that differs from a term's ordinary meaning only when it demonstrates an intent to deviate from that meaning."). The intrinsic record is replete with examples of the "providing" step being inclusive of both indirect (*e.g.*, by ingestion) and direct (*e.g.*, by infusion) providing to blood or blood plasma, and is not limited to providing by ingestion. Col. 3, lns. 10-13 ("The providing steps of the methods can include ingestion or infusion (*e.g.*, injection) of a composition . . . or a combination of ingestion and infusion."); col. 2, lns. 31-32 ("The methods include ingesting or infusing compositions into the body . . . ."); col. 5, lns. 45-47 ("The blood plasma concentrations . . . can be increased by ingestion or infusion . . . ."); col. 5, lns. 48-49 ("The composition can be administered orally, enterally, or parenterally."); J.A. at Ex. 4, Mar. 4, 1999 Petition to Make Special at 3 ("The methods of the present invention include providing the dipeptides, peptides or peptide analogues by any number of means including, for example, ingestion and injection."). Defendants' construction is derived from these statements in the intrinsic record. Moreover, Defendants' construction is consistent with Webster's definition of

"provide": "to supply or make available." Merriam-Webster's Collegiate Dictionary (10th ed. 1996) (Walter Decl. Ex. D). The plain and ordinary meaning of "providing," which is supported by the claim language and the specification, provides the proper construction.

Second, Plaintiffs' construction would violate the principle of claim differentiation. *See RF Delaware, Inc. v. Pac. Keystone Techs., Inc.*, 326 F.3d 1255, 1263 (Fed. Cir. 2003) ("[E]ach claim in a patent is presumptively different in scope."). When there is no meaningful difference between an independent claim and its dependent claim, except for an added limitation in the dependent claim, the presumption is especially strong that the independent claim is *not* restricted by the added limitation. *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 806 (Fed. Cir. 2007). Here, for example, the only difference in the '596 patent between independent claim 1 (which includes the "providing" step) and its dependent claim 7 is the added limitation that "the providing step includes ingestion of a composition including the amount of beta-alanine." '596 patent, Claims 1, 7. If Plaintiffs' construction were correct, dependent claim 7 in the '596 patent would have no meaningful difference from independent claim 1.

Third, Plaintiffs' construction obscures otherwise plain claim language without justification. For example, "providing" becomes "supplying," "effective to increase" becomes "causing an increase . . . above normal concentrations found in a typical fed state," and clumsy and inconsistent phrasing is added, *e.g.*, "by ingestion and therefore, causing . . ." and "and thereby." The purpose of claim construction is to provide clarity to the meaning of the claims from the perspective of a person of ordinary skill in the art. Plaintiffs' unsupported additions to the plain claim language serve to complicate rather then to clarify, and they should be rejected.

F. "increasing a concentration of insulin in the blood or blood plasma" ('098 Patent [claim 9]; '596 Patent [claim 9])

Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"the concentration of insulin in the blood or blood plasma is increased by ingesting or infusing insulin, or agents that stimulate the production of insulin"	"directly or indirectly increasing a concentration of insulin in the blood or blood plasma"

The dispute between the parties over the "increasing" phrase is whether the Court should deviate from the ordinary meaning of the phrase by construing it to mean increasing only by ingesting or infusing insulin or agents that stimulate the production of insulin. Defendants' construction, based directly on the claim and specification language, is the correct one.

First, nothing in the claims or intrinsic record reveal any intent of the inventors to deviate from the ordinary meaning of "increasing," or otherwise limit it to mean increasing only by ingesting or infusing insulin or agents that stimulate the production of insulin. *See, e.g., Virginia Panel Corp. v. MAC Panel Co.*, 133 F.3d 860, 865-66 (Fed. Cir. 1997) (unmodified term "reciprocating" not limited to linear reciprocation); *Bell Comms. Research v. Vitalink Comms. Corp.*, 55 F.3d 615, 621-22 (Fed. Cir. 1995) (unmodified term "associating" not limited to explicit association"); *Specialty Composites v. Cabot Corp.*, 845 F.2d 981, 987 (Fed. Cir. 1998) (unmodified term "plasticizer" given full range of ordinary and accustomed meaning). The proper construction is therefore Defendants': "directly or indirectly increasing a concentration of insulin in the blood or blood plasma." Defendants' construction is derived from unmodified claim language and statements in the intrinsic record which place no restriction on how one must "increase" insulin levels. *See, e.g.*, col. 3, lns. 14-16 ("The method can include increasing a concentration of insulin in the blood or blood plasma. The concentration of insulin can be increased, for example, by injection on insulin."); col. 5, lns. 52-54 ("The composition can include carbohydrates (*e.g.*, simply carbohydrates), insulin, or agents that stimulate the

production of insulin."). Furthermore, Defendants' construction is consistent with Webster's "increase" definition: "to make greater." Merriam-Webster's Collegiate Dictionary (10th ed. 1996) (Walter Decl. Ex. D). Although the language in Plaintiffs' construction describes exemplary embodiments of the "increasing" step, it is improper to import such limitations from the specification into the claims. *Phillips*, 415 F.3d at 1323.

Second, even if it were proper to read such limitations from the specification into the claims (it is not), Plaintiffs' construction would still be wrong because it, without justification, cherry-picks some but not all of the specification's limitations for inclusion in the proposed construction. For example, the specification explains that the composition "can include carbohydrates (*e.g.*, simple carbohydrates), insulin, or agents that stimulate the production of insulin." Col. 5, lns. 52-54. But Plaintiffs' construction recites *only* insulin and agents that stimulate the production of insulin; it *omits* carbohydrates. Another problem with Plaintiffs' construction is that the unclear phrase "agents that stimulate the production of insulin" does not help clarify the claim language but rather adds more terms likely requiring construction.

V. CONCLUSION

For the foregoing reasons, Defendants respectfully submit that their claim constructions be adopted by the Court.

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CERTIFICATE OF SERVICE

I, Francis DiGiovanni, hereby certify that on March 25, 2011, the attached document was electronically filed with the Clerk of the Court using CM/ECF which will send notification to the registered attorney(s) of record that the document has been filed and is available for viewing and downloading.

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